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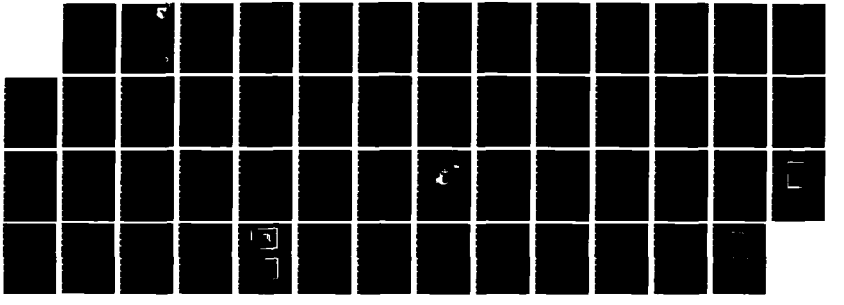

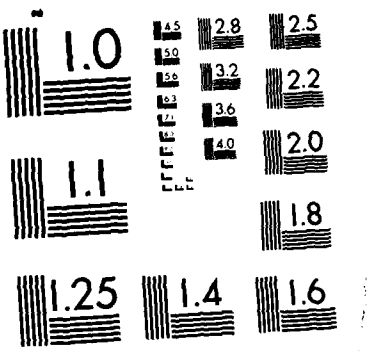

AAMRL-TR-85-060

# THE EFFECTS OF KETAMINE ON RHESUS MONKEY SKELETAL DYNAMICS

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*SEPTEMBER 1985*

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## TECHNICAL REVIEW AND APPROVAL

AAMRL-TR-83-060

The experiments reported herein were conducted according to the "Guide for the Care and Use of Laboratory Animals," Institute of Laboratory Animal Resources, National Research Council.

This report has been reviewed by the Office of Public Affairs (PA) and is releasable to the National Technical Information Service (NTIS). At NTIS, it will be available to the general public, including foreign nations.

This technical report has been reviewed and is approved for publication.

FOR THE COMMANDER

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TITLE: THE EFFECTS OF KETAMINE ON RHESUS MONKEY SKELETAL DYNAMICS. ABSTRACT: Four young male Rhesus monkeys were exposed to intramuscular injections of ketamine anesthetic (15 mg/kg) on eight selected days of a 28 day experiment. The subjects were dosed with bone labeling compounds to determine the effect ketamine had on bone modeling/remodeling dynamics. Trabecular bone sections of $T_9$ and $L_4$, and cortical bone sections of proximal femur and midshaft femur were used for histomorphometric analysis. Urine creatinine and calcium, and serum alkaline phosphatase and calcium levels were determined. Vertebral centrum compression tests were conducted on selected thoracic and lumbar levels. Stiffness, ultimate load and modulus showed significant increases in the ketamine exposure group. The results of the trabecular histomorphometry showed a possible increase in mineralization lag time or slower mineralization. Cortical bone histomorphometry could indicate activation of the skeletal system. The experimental results lead to the conclusion that something affected the mechanical strength parameters and the bone remodeling dynamics of the ketamine exposure group. It is unclear as to whether these differences are strictly due to (cont.)

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18 cont.

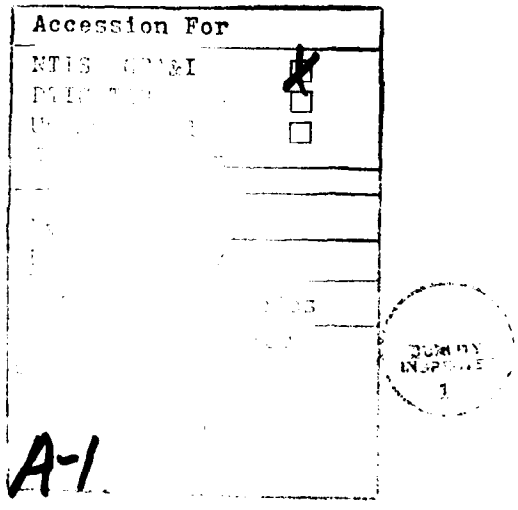
alkaline phosphatase
serum, urine calcium
creatinine
Rhesus monkey

19 cont.

ketamine as stress and age difference were other influencing factors.

SUMMARY

The effect of ketamine anesthetic on Rhesus monkey bone dynamics was investigated. Biochemical, biomechanical and histological analysis was conducted following a 28 day exposure with eight ketamine injections. Biochemical analysis included urine and serum calcium, urine creatinine and serum alkaline phosphatase. Vertebral centrum compression tests and disc hydration analysis were completed and analyzed by Analysis of Variance statistical method. Stiffness, ultimate load and modulus showed significant increases in the ketamine exposure group. Tissue sections of selected trabecular and cortical bone were analyzed for various histomorphometric parameters. The results of the trabecular histomophometry showed a possible increase in mineralization lag time or slower mineralization. Cortical bone histomorphometry could indicate activation of the skeletal system. The experimental results lead to the conclusion that something affected the mechanical strength parameters and the bone remodeling dynamics of the ketamine exposure group. It is unclear as to whether these differences are strictly due to ketamine as stress and age difference were other influencing factors.



## PREFACE

This work was accomplished under Project 72311416, "Biomaterials and Kinematics," and was performed in the Biodynamic Effects Branch, Biodynamics & Bioengineering Division, Harry G. Armstrong Aerospace Medical Research Laboratory.

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## INTRODUCTION

Ketamine hydrochloride (Parke-Davis) is an anesthetic that is widely used in veterinary medicine. Its use has been described in a variety of species including subhuman primates (2,3,5,9,10,11,23). Ketamine is classified as a cataleptoid anesthetic and analgesic agent that acts on the central nervous system (CNS) to selectively interrupt sensory neuronal pathways between the CNS and peripheral areas of the body. The anesthetic state induced by the drug is termed "dissociative" anesthesia (5,6,14) and the patient is deeply anesthetized while appearing to be in only a superficial state of sleep.

There have been many reports published concerning the effects of ketamine on electrolytes (24), cerebral spinal fluid pressure (30), EEG activity (11,20), hemodynamics (12) and blood sugar levels (13). To date, no one has investigated its possible effects on bone metabolism.

Fahringer et al. (15) reported that ketamine was a potent stimulator of the adrenocortical system in rats, causing an approximately 8-fold increase in the hormone corticosterone within 20-30 minutes of administration. Further, Oyama et al. (29) have reported that ketamine-nitrous oxide - oxygen anesthesia alone significantly stimulated adrenocortical activity in humans. Kemnitz and Kraemer (23) investigated the effects of ketamine on glucoregulation in rhesus monkeys. They concluded that there was a relatively small, probably physiologically unimportant elevation of serum cortisol, another adrenocortical hormone.

The complete effects of these steroid hormones on bone metabolism are not known, however, osteoporosis is a major problem associated with long-term steroid treatment as well as increased levels of steroid hormones (4). Adrenocortical hormones have been shown to inhibit formation of collagen and glycosaminoglycans, both of which are components of bone and cartilage extracellular matrix (4,33,34). It is therefore possible that the steroid hormones interfere with bone formation by reducing the surface on which bone mineral can be deposited (6).

Ketamine is often used as the anesthetic of choice in animal studies, including those investigating various aspects of bone metabolism. Due to the potential for interference, the present study was undertaken to investigate the effects of recommended normal doses of ketamine on selected bone metabolic parameters as determined by histomorphometric techniques.

## MATERIALS AND METHODS

Four young male Rhesus monkeys (Macaca mulatta) were used as test subjects. The subject identification numbers, ages and body weights are as follows:

| | | |
|---|---|---|
| Y8296 | 5 yr. 7 mo. | 5.0 kilograms |
| 0F8 | 2 yr. 8 mo. | 4.4 kilograms |
| 03Y | 3 yr. 7 mo. | 4.8 kilograms |
| 03T | 3 yr. 4 mo. | 4.9 kilograms |

The animals were housed in metabolic cages for the duration of the 28 day exposure. This exposure consisted of intramuscular ketamine injections at a 15 mg/kg level given on days E-1 and 0 (initiation of the experiment) and on days 6, 7, 13, 14, 20 and 21. Blood was collected at day 0 and every 7 days thereafter. Radiographs were taken prior to the initiation of the study and every 7 days thereafter. In preparation for the histomorphometric analysis, the animals were given Declomycin (Lederle Laboratories Division, American Cyanamid Co., Pearl River NY) at E-1 and zero days and days 6 and 7. Tetracycline (Pfizer Laboratories Division, Pfizer Inc., NY) was given on days 13, 14, 20 and 21. Declomycin and tetracycline HCL are bone tagging hydrochloride compounds that make it possible to determine modeling and remodeling of bone by virtue of their fluorescence under ultraviolet light. Urine samples and fecal samples were collected daily and frozen for later analysis. General health, diet and the activity of each animal was recorded daily. The animals were sacrificed on days 29 and 30 to collect tissue samples.

The control animals utilized in the study were also the control animals for the study "Effects of Acute Hypogravic Exposure and Recovery on the Vertebral Column of Juvenile Primates (Macaca Mulatta)" (16). The identification numbers, ages and body weights are as follows:

| | | |
|---|---|---|
| OAI | 2 yr. 10 mo. | 4.0 kilograms |
| 039 | 2 yr. 8 mo. | 3.9 kilograms |
| 038 | 2 yr. 8 mo. | 3.2 kilograms |

The control animals were housed in metabolic cages for 28 days. These control animals were treated the same as the exposure animals with exception only of the ketamine injections.

Biomechanical testing

Vertebral centrum compression tests were conducted on thoracic levels of 2, 3, 5, 6, 7, 10, 11, 12 and lumbar levels of 1, 2, 3, 5 and 6. The compression techniques as described by Kazarian (21) were used. Preparation for testing included removal of all surrounding soft tissue, including muscle, ligaments and intervertebral disc material and by removal of the posterior process at the base of the pedicle. The centra's posterior and anterior heights were measured, and photographs of end plate surfaces were taken. Polymethylmethacrylate was used to form thin pots for the superior and inferior surfaces of each centrum. Compression tests were performed using a MTS Universal Testing System equipped with a 5 KN load cell. The vertebral centra were compressed to 50% of original height at constant displacement of 210 in/min. Load vs. displacement test data was stored. This raw data, combined with average centrum height and centrum area was reduced to provide various engineering parameters. To aid in data reduction and statistical comparison, the vertebral centra used for the compression testing were grouped as follows: P1=$T_2$ $T_3$, P2=$T_5$ $T_6$ $T_7$, P4=$T_{10}$ $T_{11}$ $T_{12}$, P5=$L_1$ $L_2$ $L_3$ and P6=$L_5$ $L_6$. The prepared specimens were tested within 2-6 hours following sacrifice of the animal.

## Disc hydration analysis

Intervertebral disc hydration analysis was used to measure gross structural properties and to determine total percent weight water loss and water weight percent loss per disc volume. Discs from the spinal thoracic levels $T_{4-5}$, $T_{7-8}$, $T_{9-10}$, $T_{11-12}$ and lumbar levels $L_{1-2}$, $L_{4-5}$, $L_{6-7}$ were removed and stripped of all muscle tissue. The discs were photographed and anterior and posterior heights were measured. The discs were then placed in a desiccation chamber and weighed once a week until there was no further weight loss. Biomechanical tests for all control and exposure subjects were conducted in the same method.

## Biochemical analysis

Urine creatinine and calcium, along with serum alkaline phosphatase and serum calcium levels were determined. Test methodology for all tests used a DuPont colorimetric discrete clinical analyzer. The calcium (urine and serum) analysis utilized a modification of the calcium D-cresolphthalein complex one (OCPC) complexometric reaction (1). Creatinine analysis employed a modification of the Jaffe reaction (25). Selected samples were analyzed, those being: 0, 6, 13, 20 and 26 or 27 days. The analysis was completed by the Toxic Hazards Division at the Aerospace Medical Research Laboratory. The analysis of the control samples was conducted by Pollution Control Sciences, Inc. and different methods were sometimes used. Serum alkaline phosphotase activity was measured with the Cezurichrome Alkaline Phosphotase Reagent System and determined colorimetrically. Urine creatinine was analyzed by the Jaffe reaction and analyzed colorimetrically. Calcium (serum and urine) content analysis was performed with flame atomic absorption spectrophotometry. The control samples were collected on the same days as those from the exposure subjects.

## Histomorphometry

Tissue sections were taken from midshaft right femur, proximal right femur, and midsagittal vertebral thoracic level nine and midsagittal lumbar level four. The location of midshaft femur sections was 1/2 the length from the greater trochanter to the femoral condyles. Proximal femur tissue sections were 0.5 cm in length and were located 1 cm distal to the tip of the lesser trochanter. Thoracic 9 ($T_9$) and lumbar 4 ($L_4$) samples were embedded in methyl methacrylate prior to sectioning (32). Four sections of vertebral and femoral bone tissues were cut to 200 um using an Isomet bone saw. These sections were ground to 30-60 um thick using carborundum abrasive paper under running water. The cortical bone sections were mounted with Permount mounting medium (Fisher Scientific Inc., Cincinatti OH); Villanueva's bone staining technique was used to stain the trabecular bone sections (8,32). These were mounted on slides with Euparal adhesive (Roboz Surgical, Washington DC).

Several histomorphometric measurements could not be measured due to the labeling technique. There were four labels given, but the difference between tetracycline and declomycin was indistinguishable. Therefore, on the cortical sections if only two labels were seen, it was not known if these two were the first two, the middle two, or the last two labels. The trabecular tissue sections appeared so diffuse, it was impossible to determine the edge of the label.

Histomorphometric analysis of the cortical bone was conducted with Frost's "point count" method utilizing a calibrated ocular grid. (17,18) Total cortical bone area was determined with a dissection microscope at 11.1X magnification. A Zeiss Photomicroscope I (Carl Zeiss Inc, Thornwood NY) equipped with a mercury illuminator for reflected and transmitted light at 160X magnification was used for the remaining measurements. Each cortical bone section was divided into four equal quadrants, (posterior, anterior, medial, lateral) determined by positioning the linea aspera centrally in the posterior quadrant. Parameters determined were bone cross sectional area ($A_c$), number of osteoid seams per area ($A_f$), number of resorption spaces per area ($A_r$), mean wall thickness of finished osteons (mwt) and circumference of osteoid seams ($S_f$).

Trabecular bone sections were analyzed using a computerized data acquisition system with image digitizer developed by Malluche and Manaka (26,27). This system is based on the same principles as the ocular grid method, but much more accurate as the digitizer grid mesh size is much smaller than the ocular grid. Because the accuracy is increased a smaller sample size may be taken. For all trabecular bone measurements a Zeiss research compound bionocular microscope equipped with a halogen lamp and a 9901 blue film fluorescence unit at 10X magnification was used. Due to the accuracy of this system, only one prepared midsagittal bone section from each $T_9$ and lumbar $L_4$ was analyzed. The thoracic vertebral section was divided into two analysis sites: inferior and superior, six fields long by three fields deep. The lumbar vertebral section was divided into four analysis sites: inferior, superior, anterior and posterior. The inferior and superior analysis sites consisted of five fields long by five fields deep. The anterior and posterior sites consisted of two fields long by six fields deep. The analysis sites were located away from the vertebral centra's perimeters to ensure exclusion of woven bone. The analysis included results for the following parameters: volumetric density of bone, VV ($mm^3/cm^3$), surface density of bone, SV ($mm^2/cm^3$), mean trabecular diameter, DTRAB (mm), volumetric density of lamellar osteoid, VVOS ($mm^3/cm^3$), thickness of lamellar osteoid, THOS (um), percent of trabecular surface covered by lamellar osteoid, OSI (%), relative volumetric density of osteoid, VVOI ($mm^3/cm^3$), and percent of trabecular surface exhibiting Howship's lacunae, HL (%).

RESULTS

The mechanical properties of the vertebral bodies were compared using the two way analysis of variance (ANOVA) for a p x q factorial experimental design. Dunnett's t test was used to test the means between experimental and control values. The student's t test was used to determine significant variation between means of the same exposure group.

The following figures (1-11) are the graphical results of the vertebral centrum compression tests with column position on the abscissa and the resulting strength parameter on the ordinate. The points on the curves represent the average value from the vertebral level group (i.e., P1, P2, P4, P5, P6). An asterisk (*) next to the curve represents a significant difference ($\alpha$=0.05) between the ketamine exposure group (RK) and the control group (RC). The lower vertebral bodies (P4, P5 and P6) of the ketamine exposure group had significantly ($\alpha$=.05) greater surface areas and vertebral body heights. (See Appendix)

# VERTEBRAL CENTRUM COMPRESSION TESTS

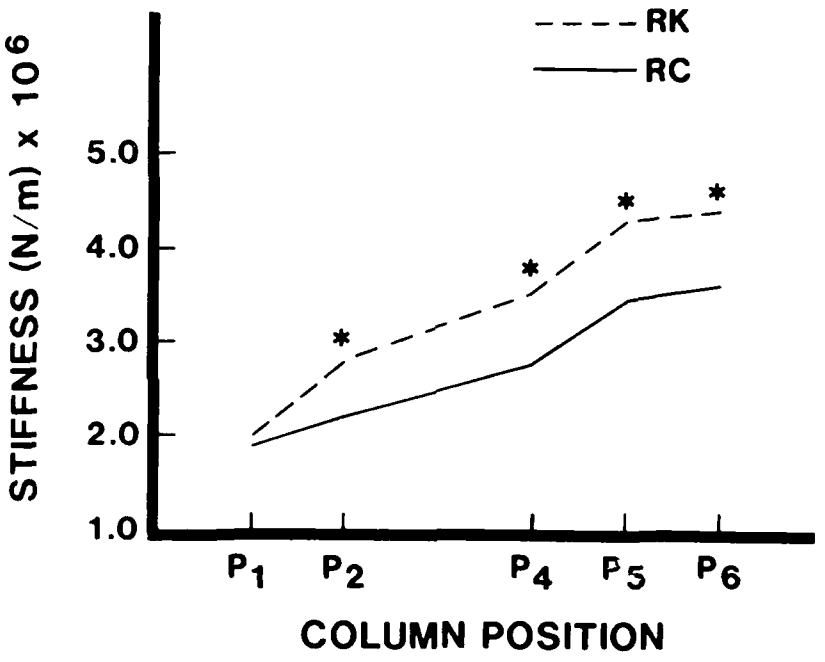


Figure 1

# VERTEBRAL CENTRUM COMPRESSION TESTS

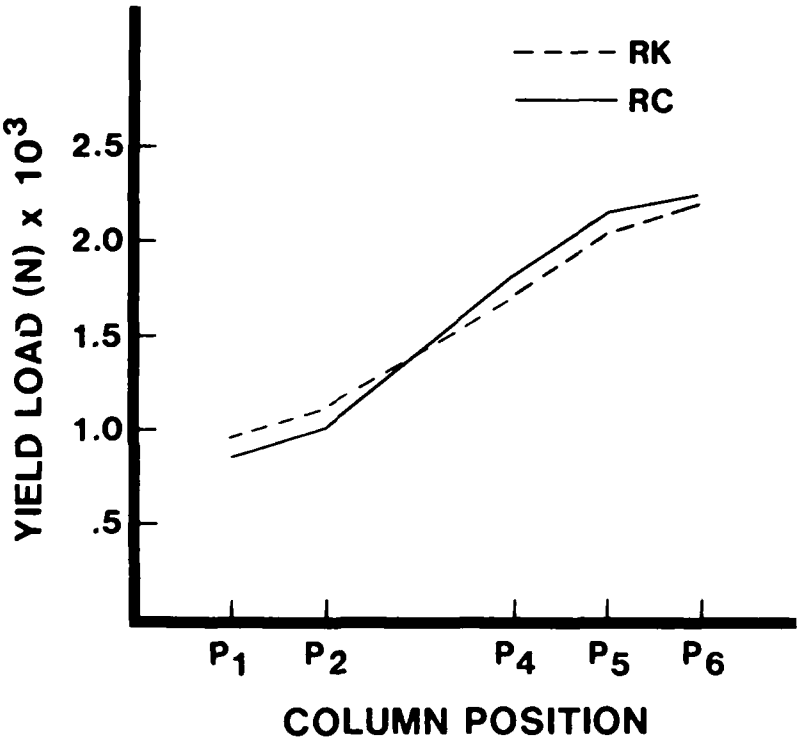


Figure 2

# VERTEBRAL CENTRUM COMPRESSION TESTS

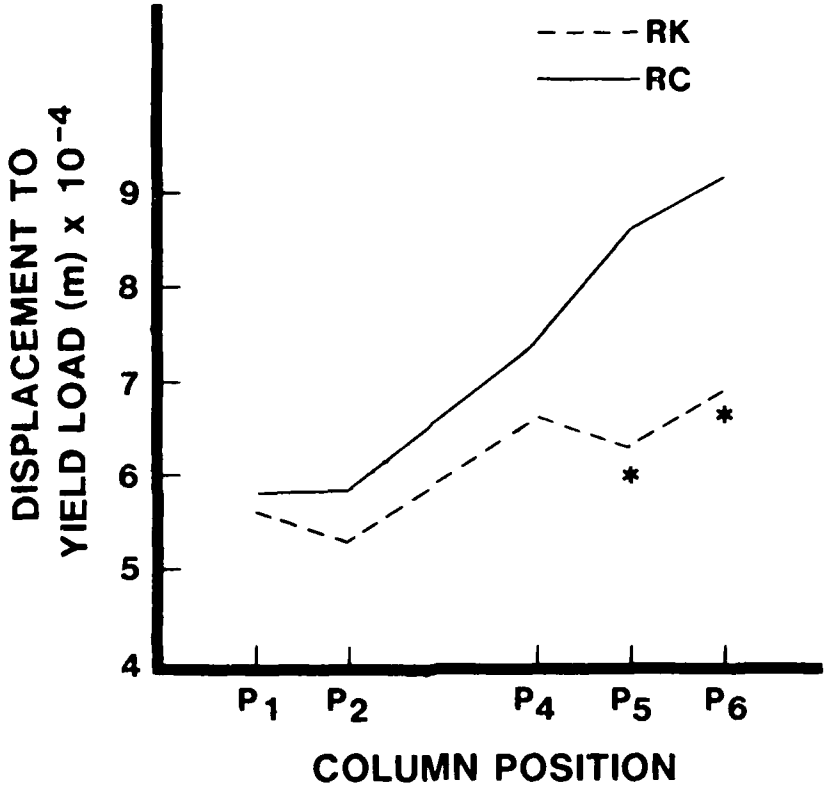


Figure 3

# VERTEBRAL CENTRUM COMPRESSION TESTS

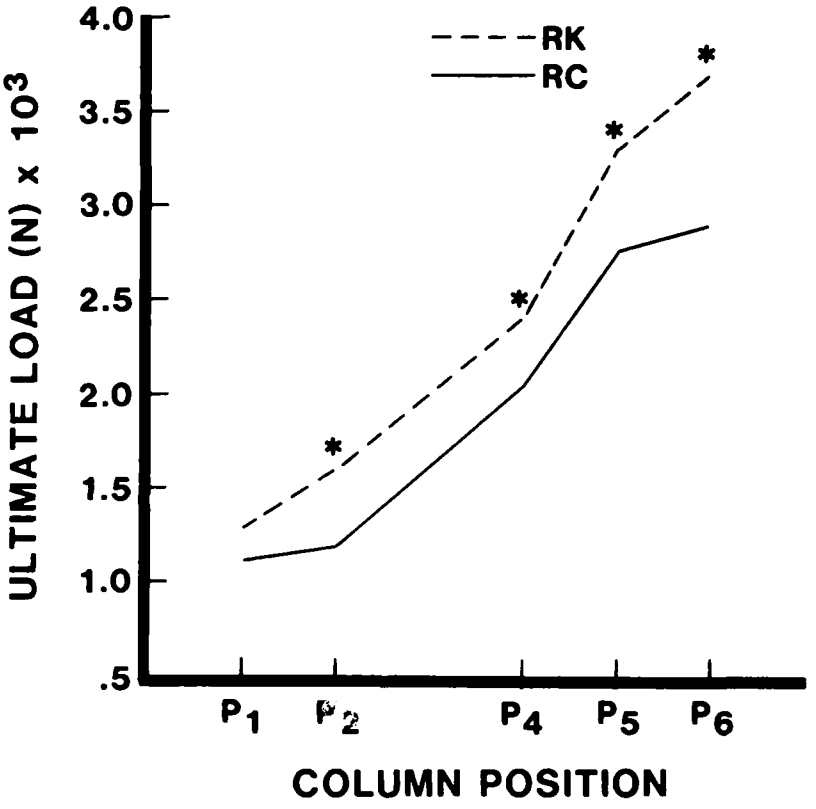


Figure 4

# VERTEBRAL CENTRUM COMPRESSION TESTS

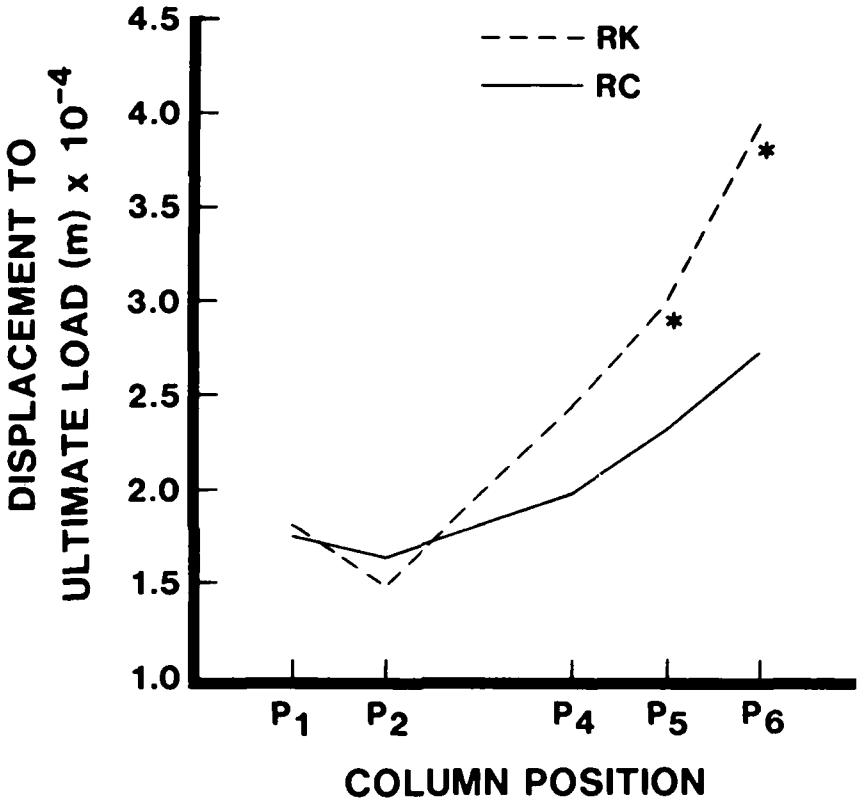


Figure 5

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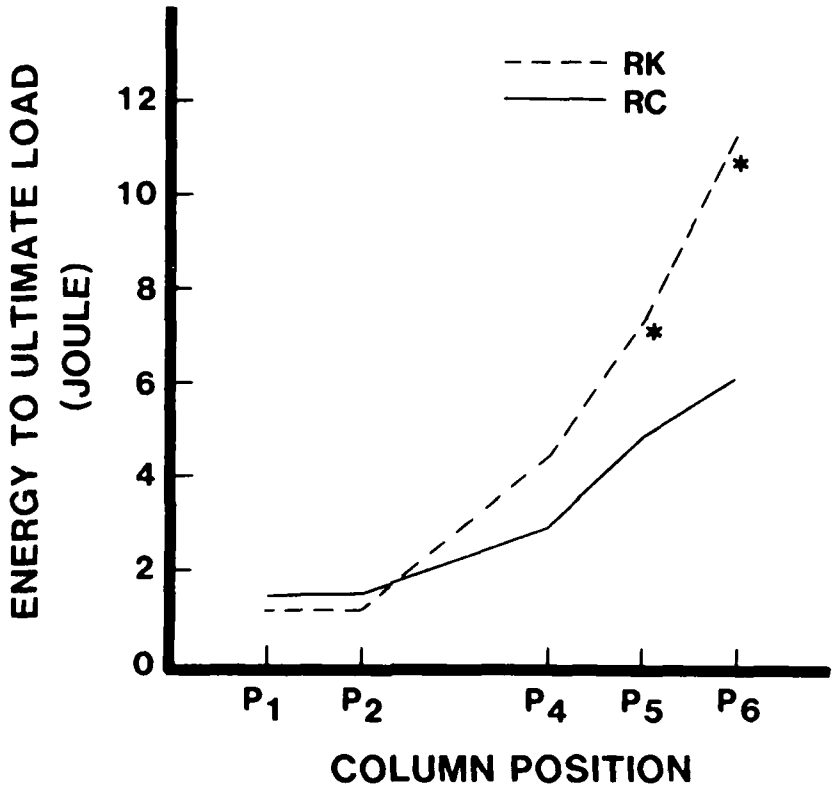


Figure 6

# VERTEBRAL CENTRUM COMPRESSION TESTS

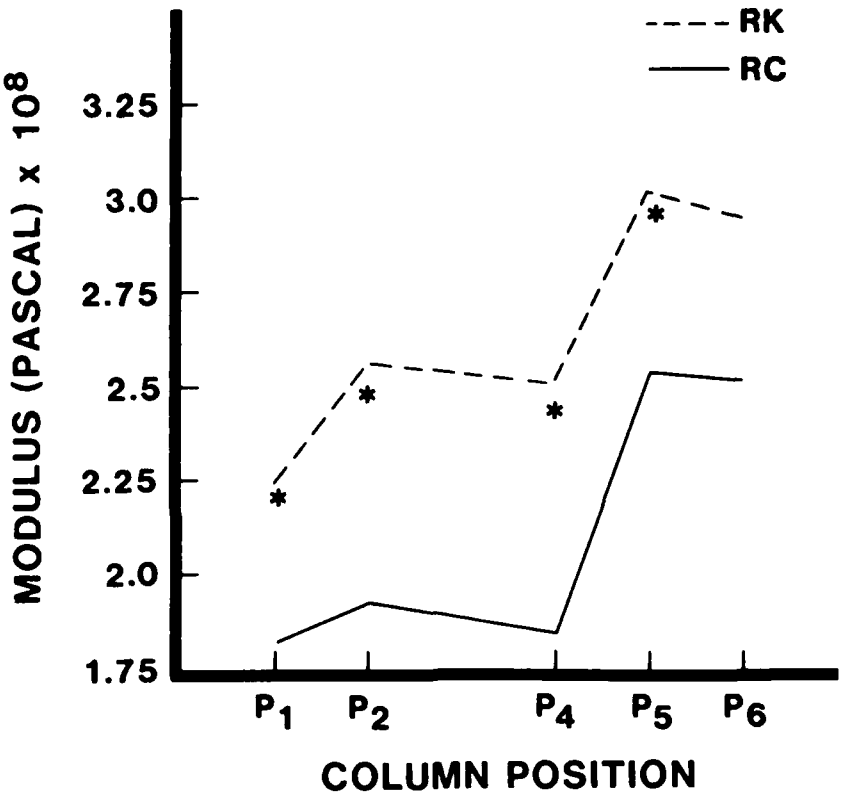


Figure 7

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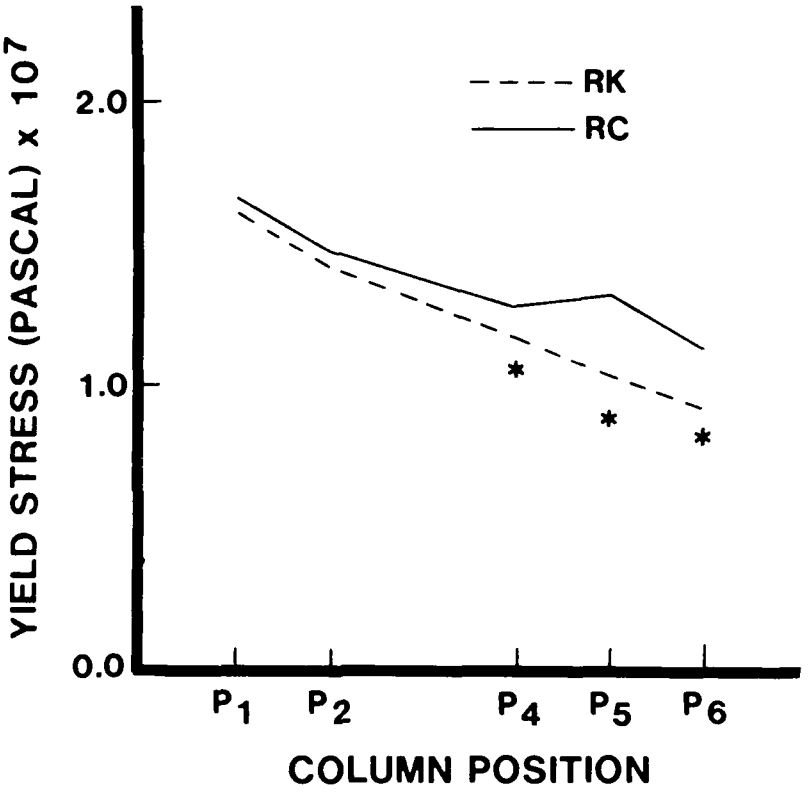


Figure 8

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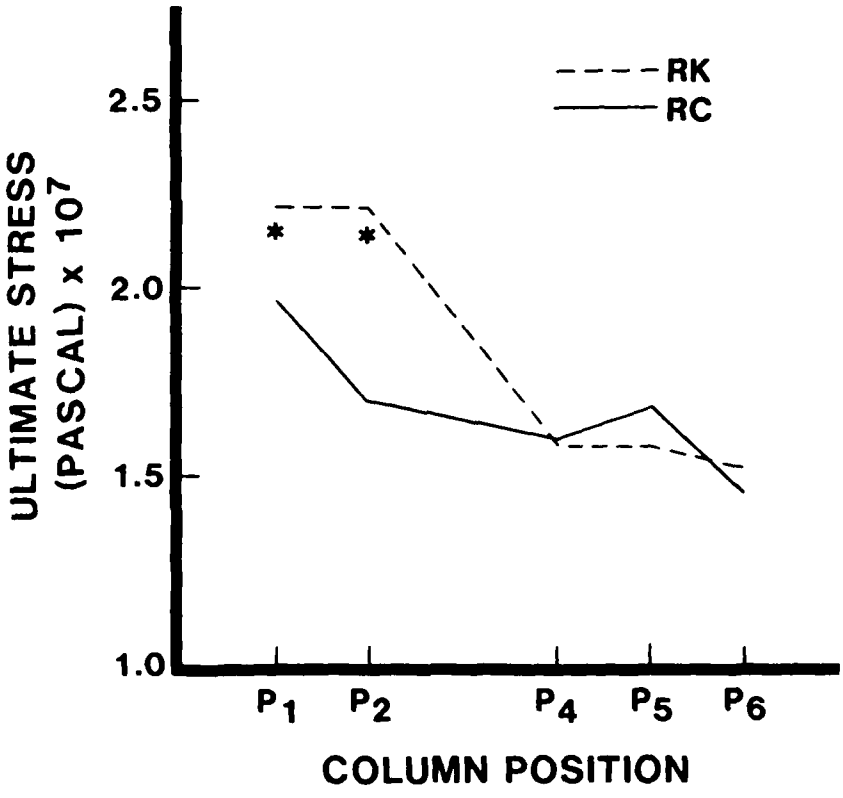


Figure 9

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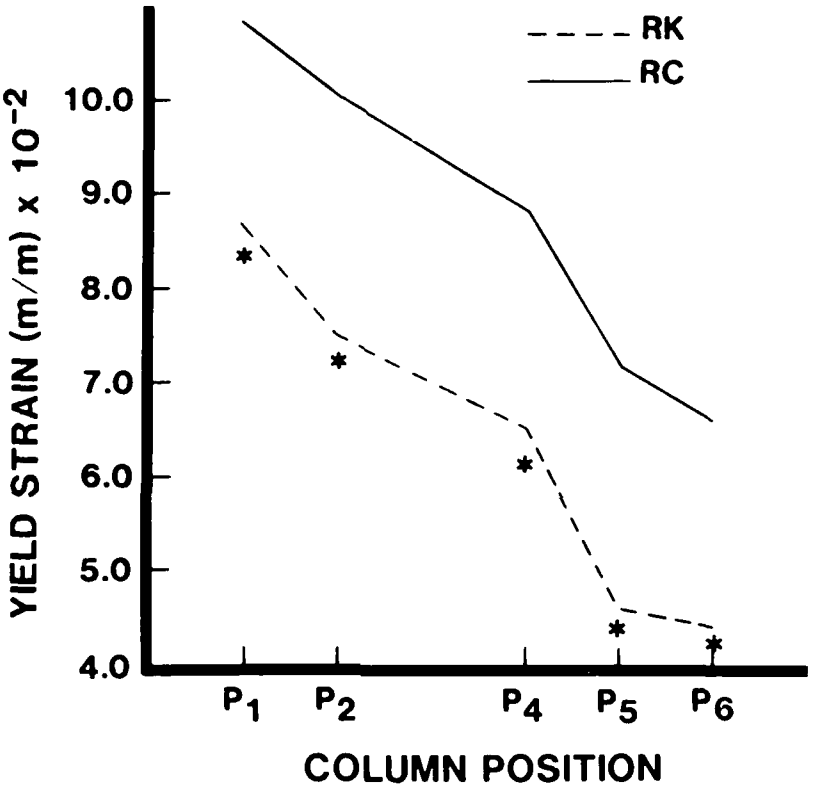


Figure 10

# VERTEBRAL CENTRUM COMPRESSION TESTS

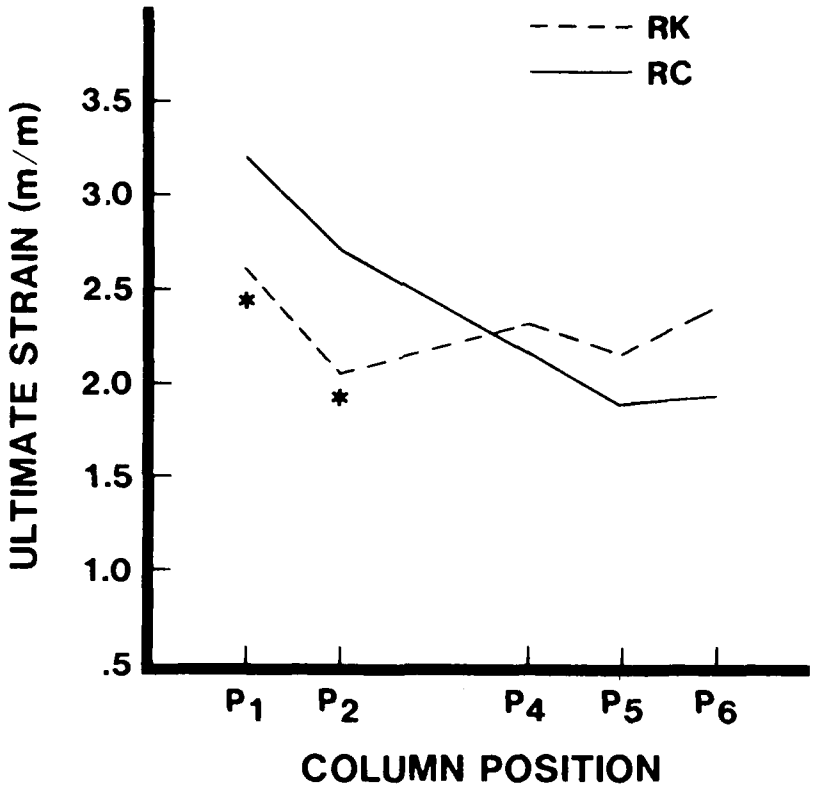


Figure 11

The results of the biochemistry are listed in Table 1. The alkaline phosphatase results showed a significant difference between the ketamine exposure and the control group, with the ketamine exposure having increased values (student's t test, $\alpha$ =0.05). Serum calcium was significantly lower (student's t test, $\alpha$=0.05) in the ketamine exposure group. There were no significant differences in the urine creatinine or the urine calcium results.

| PARAMETER | RK | | | RC | | |
|---|---|---|---|---|---|---|
| | X | S | N | X | S | N |
| Alkaline Phosphatase (U/L) | 467 | 125.1 | 20 | 364 | 65.1 | 14 |
| Serum Calcium (mg/dL) | 9.13 | 0.56 | 20 | 10.6 | .89 | 13 |
| Urine Calcium (mg/24 hrs) | 123.46 | 84.24 | 22 | 167 | 102.8 | 24 |
| Urine Creatinine (mg/24 hrs) | 139.31 | 150.02 | 22 | 192 | 131.4 | 42 |

Table 1 - Biochemical Content Analysis, Mean (X), Standard Deviation (S) and Sample Number (N)

The results of the cortical bone histomorphometry indicate a significant difference in the totals of four of the five parameters and are shown in Table 2. Within the individual quadrants there are variations. Bone cross sectional area significantly increased in three quadrants: anterior, posterior and medial. The number of osteoid seams increased in the medial quadrant. The number of resorption spaces significantly increased in the anterior quadrant and significantly decreased in the lateral quadrant. Mean wall thickness significantly decreased in the lateral quadrant with a non-significant decrease in the other three quadrants. Circumference of osteoid seams decreased in all quadrants with a significant decrease only in the medial quadrant. The lateral quadrant seemed to provide values most unlike the other quadrants. If the lateral values were excluded the total number of resorption spaces increased significantly.

| PARAMETER | ANT. | POST. | MED. | LAT. | TOT. |
|---|---|---|---|---|---|
| Bone cross sectional area mm ($A_c$) CCAS | ↑* | ↑* | ↑* | - | ↑* |
| No. osteoid seams/mm ($A_f$) OS/UAB | - | - | ↑* | - | ↑* |
| No. resorption spaces/mm ($A_r$) RS/UAB | ↑* | - | - | ↓* | - |
| Mean wall thickness, mm (mwt) | - | - | - | ↓* | ↓* |
| Circum. of osteoid seam, mm ($S_f$) MC/OS | - | - | ↓* | - | ↓* |

*Statistically significant ($\alpha$=0.05 student's t test)
↑ Indicates increase as compared to control group (RC)

↓ Indicates decrease as compared to control group (RC)

Table 2 - Results of Cortical Bone Histomorphometry

The results of the trabecular bone histomorphometry are presented in Tables 3 and 4. Most of the parameters for the different quadrants proved to be significantly different in the ketamine exposure group as compared to the control group. For the lumbar level, the volumetric density of bone (VV) significantly decreased in all quadrants (ANOVA $\alpha$=0.05). The thickness of lamellar osteoid (THOS) significantly increased in all quadrants. In three quadrants (posterior, superior and inferior) percent of trabecular surface covered by lamellar osteoid (OSI) decreased significantly. Other than those discussed above, there was little consistency within each parameter.

In thoracic level 9, volumetric density of bone (VV), surface density of bone (SV) and percent of trabecular surface covered by lamellar osteoid (OSI) decreased significantly in both superior and inferior quadrants. Significant increases occurred in thickness of lamellar osteoid (THOS), relative volumetric density of osteoid (VVO) and percent of trabecular surface exhibiting Howship's lacunae (HL) in both the superior and inferior quadrants.

| PARAMETER | ANT. | POST. | SUP. | INF. |
|---|---|---|---|---|
| VV ($mm^3/cm^3$) | ↓* | ↓* | ↓* | ↓* |
| SV ($mm^2/cm^3$) | ↑* | - | ↓* | ↓* |
| D-TRAB (mm) | ↓* | ↓* | - | - |
| VVOS ($mm^3/cm^3$) | ↑* | - | - | ↓* |
| THOS (um) | ↑* | ↑* | ↑* | ↑* |
| OSI (%) | - | ↓* | ↓* | ↓* |
| VVO ($mm^3/cm^3$) | ↑* | ↑* | - | ↓* |
| HL (%) | - | ↓* | - | ↑* |

* Indicates significant difference (ANOVA, $\alpha$=0.05)

↑ Indicates increase as compared to control group (RC)

↓ Indicates decrease as compared to control group (RC)

Table 3 - Results of Trabecular Bone Histomorphometry Lumbar 4 Midsagittal Vertebral Centrum Analysis

| PARAMETER | SUP. | INF. |
|---|---|---|
| VV ($mm^3/cm^3$) | ↓* | ↓* |
| SV ($mm^2/cm^3$) | ↓* | ↓* |
| D-TRAB (mm) | - | ↓* |
| VVOS ($mm^3/cm^3$) | ↑* | - |
| THOS (um) | ↑* | ↑* |
| OSI (%) | ↓* | ↓* |
| VVO ($mm^3/cm^3$) | ↑* | ↑* |
| HL (%) | ↑* | ↑* |

* Indicates significant difference (ANOVA, $\alpha$=0.05)
↑ Indicates increase as compared to control group (RC)
↓ Indicates decrease as compared to control group (RC)

Table 4 - Results of Trabecular Bone Histomorphometry Thoracic 9 Midsagittal Vertebral Centrum Analysis

Intervertebral disc hydration analysis resulted in little difference in anterior height or posterior height between the ketamine exposure group and the controls. Percent water weight loss was only significantly different at levels $T_{4-5}$ and $T_{9-10}$. The parameter percent water weight loss per volume indicated significantly lower values for all thoracic intervertebral discs and upper lumbar intervertebral discs.

## DISCUSSION AND CONCLUSION

The results of this experiment lead to some interesting assumptions but few conclusive statements. One of the greatest problems was found to be in the different geometry of the vertebral bodies. The control animals were juveniles and the ketamine exposure group varied from juvenile to young adult. Primate and human age comparisons indicate that one monkey year is equivalent to 3.5 human years (31), therefore, a difference of two years between the control animals and exposure animals can be quite significant. This difference was evident in the vertebral body areas and vertebral body heights, where the lower thoracic and lumbar values were significantly greater ($\alpha$=0.05) in the ketamine exposure group. This difference affects the vertebral centrum compression tests, but to what degree is unclear. A plot of the ratio of vertebral body area to vertebral body height showed a close correlation at P1, P2 and P4, but a significant difference at the lumbar levels.

# VERTEBRAL BODY AREAS/HEIGHTS

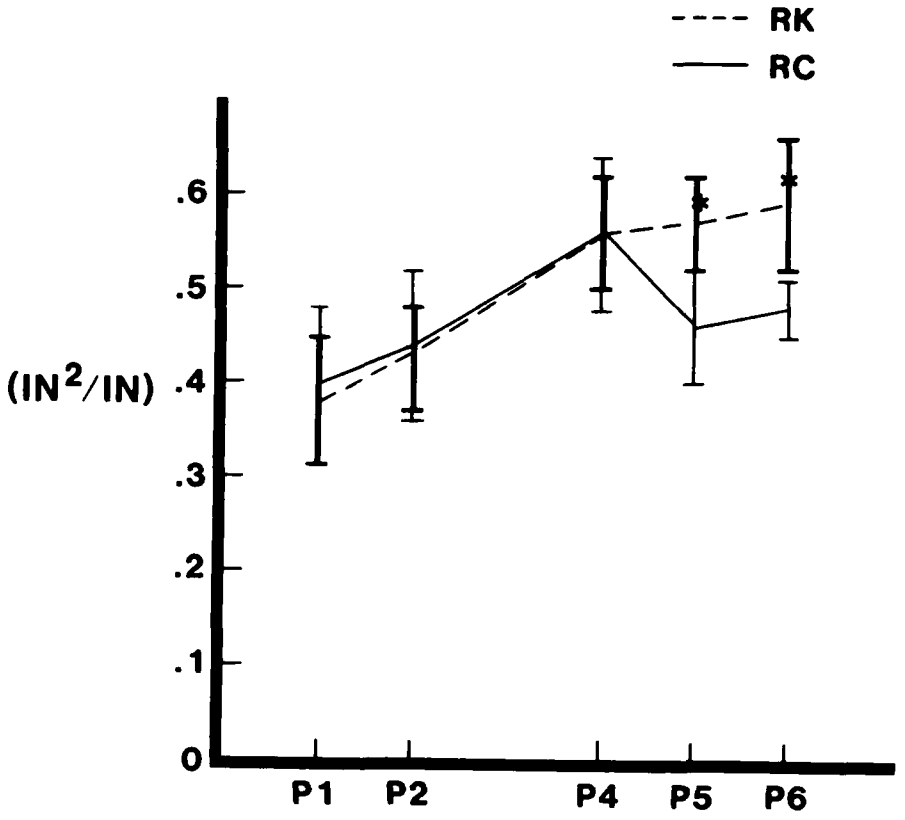


Figure 12

Using this as a guideline, the vertebral centrum compression test parameter differences in the thoracic region seem to be due to something other than geometry, while the parameter differences in the lumbar region were probably influenced by vertebral body geometry as well as other factors. The above plot of the ratio of vertebral body areas to vertebral body heights also suggests that in the younger animals (RC) the vertebral body heights increased at a faster rate than the vertebral body areas at that level. The ketamine exposure group (RK) was just enough older that vertebral body areas had probably increased sufficiently to make up the lag time between the growth of the area and the height. This observation could be related to the fact that in growing animals the epiphiseal plates of the thoracic region close sooner than in the lumbar region (22).

Looking only at the thoracic level results of the vertebral centrum compression tests, the ketamine exposure group had greater stiffness, ultimate stress and ultimate load. Modulus, the value normalized by area/height indicates significant differences in all thoracic levels with higher values for the ketamine exposure. These differences in the thoracic levels may be related to the internal structure. The age difference between the two groups may be the cause of the strength parameter differences.

The trabecular bone, indicated by the histomorphometry did show significant differences between control and experimental values. The density, surface volume and the diameter of the trabeculae decreased. The thickness of lamellar osteoid increased although the percent of trabecular surface covered by lamellar osteoids decreased indicating perhaps an increased mineralization lag time or slower mineralization. This could not be confirmed, however, because several parameters could not be measured. These internal differences may have affected the strength parameters, i.e. thicker lamellar osteoid giving higher stiffness, modulus, ultimate stress or ultimate load values.

The cortical bone histomorphometry results could indicate activation of the skeletal system. The Activation→ Resorption→ Formation (A→ R→ F) (18) sequence could have been triggered or here again age may be the greatest influencing factor. There is an increase in resorption spaces perhaps leading to the observed increase in osteoid seams, but the circumference of these osteoid seams is decreased. The increase in resorption spaces may be prevalent in the RK group because these older animals have reached the bone remodeling stage. The skeletons of younger control group animals (RC) may still be modeling which is normal during the growing years. Alkaline phosphatase, an indicator of osteoblastic activity (19), increased in the RK group. This supports the theory of the triggering of the A→ R→ F sequence. The increase in serum calcium was significant but there was no body loss of calcium, because urine calcium showed no change.

Another factor complicating interpretation of the results is the fact that the control animals were given no anesthetic, thus all procedures were done under purely physical restraint. Corticosteroid response, as reported by Mason (28) increased threefold when Rhesus monkeys were stressed by being placed in restraining chairs. The effect was acute, only lasting three days. The control animals in this study could have been affected likewise, as they were carried to different rooms for radiographs, blood withdrawal and tetracycline adrenocortical injection. The amount of stress that these animals perceived is unknown and hormone levels were not measured. However, stated in the introduction, increased steroid levels are associated with altered bone metabolism resulting in osteoporosis (4).

The experimental results lead to the conclusion that something affected the mechanical strength parameters and the bone remodeling dynamics of the ketamine exposure group. It is unclear what might have caused this: the ketamine, the stress (i.e. hormone production) or the age difference. It appears that the age difference between the exposure group and the control group was too great. In future bone modeling/remodeling studies it is suggested that, animal subjects within 2 months of the same age should be chosen if these animals are still growing (under 4 years old). In mature animals there is less of a problem, but in adolescent or juvenile animals the individual variations in bone dynamics are too great. Additionally, hormone levels should be measured to determine the effect stress has on the adrenocortical system, as the increased production of hormones can adversely affect bone modeling/remodeling dynamics.

# APPENDIX

| N | Subject ID | CP | VB Level | Displacement Rate m/s | Pretest Length m | Pretest Average Area sq.m | Modulus Pascal | Engineering Yield Stress Pascal | Engineering Yield Strain m/m | Ultimate Engineering Stress (Body) Pascal | Ultimate Engineering Strain (Body) m/m |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 101 | RH-0F8 | 1 | T1 | 8.890E-02 | 5.080E-03 | 5.972E-05 | 1.540E+08 | 1.236E+07 | 9.869E-02 | 1.785E+07 | 2.974E-01 |
| 102 | RH-0F8 | 2 | T2 | 8.890E-02 | 5.842E-03 | 5.262E-05 | 2.163E+08 | 1.562E+07 | 8.452E-02 | 2.090E+07 | 2.791E-01 |
| 103 | RH-0F8 | 3 | T3 | 8.890E-02 | 6.096E-03 | 5.325E-05 | 2.538E+08 | 1.698E+07 | 8.533E-02 | 2.158E+07 | 2.843E-01 |
| 104 | RH-0F8 | 5 | T5 | 8.890E-02 | 6.096E-03 | 6.467E-05 | 2.753E+08 | 1.586E+07 | 6.350E-02 | 1.818E+07 | 2.843E-01 |
| 105 | RH-0F8 | 6 | T6 | 8.890E-02 | 6.604E-03 | 6.494E-05 | 2.455E+08 | 1.600E+07 | 7.770E-02 | 1.960E+07 | 1.258E-01 |
| 106 | RH-0F8 | 7 | T7 | 8.890E-02 | 6.858E-03 | 7.236E-05 | 3.791E+08 | 1.567E+07 | 5.908E-02 | 1.974E+07 | 1.072E-01 |
| 107 | RH-0F8 | 10 | T10 | 8.890E-02 | 8.636E-03 | 1.105E-04 | 2.853E+08 | 1.425E+07 | 6.904E-02 | 1.772E+07 | 2.227E-01 |
| 108 | RH-0F8 | 11 | T11 | 8.890E-02 | 9.652E-03 | 1.252E-04 | 2.595E+08 | 1.175E+07 | 5.878E-02 | 1.557E+07 | 2.713E-01 |
| 109 | RH-0F8 | 12 | T12 | 8.890E-02 | 1.016E-02 | 1.582E-04 | 1.950E+08 | 9.589E+06 | 6.253E-02 | 1.412E+07 | 2.100E-01 |
| 110 | RH-0F8 | 13 | L1 | 8.890E-02 | 1.143E-02 | 1.720E-04 | 2.126E+08 | 1.031E+07 | 6.875E-02 | 1.584E+07 | 2.454E-01 |
| 111 | RH-0F8 | 14 | L2 | 8.890E-02 | 1.219E-02 | 1.824E-04 | 3.469E+08 | 1.158E+07 | 4.831E-02 | 1.509E+07 | 1.743E-01 |
| 112 | RH-0F8 | 15 | L3 | 8.890E-02 | 1.295E-02 | 2.022E-04 | 3.770E+08 | 1.140E+07 | 3.941E-02 | 1.511E+07 | 2.071E-01 |
| 113 | RH-0F8 | 17 | L5 | 8.890E-02 | 1.346E-02 | 2.293E-04 | 3.430E+08 | 1.183E+07 | 4.660E-02 | 1.489E+07 | 2.207E-01 |
| 114 | RH-0F8 | 18 | L6 | 8.890E-02 | 1.295E-02 | 2.272E-04 | 2.953E+08 | 1.076E+07 | 5.853E-02 | 1.372E+07 | 2.664E-01 |
| 115 | RH-03T | 1 | T1 | 8.890E-02 | 5.842E-03 | 5.933E-05 | 1.378E+08 | 1.419E+07 | 1.344E-01 | 5.317E+07 | 2.964E-01 |
| 116 | RH-03T | 2 | T2 | 8.890E-02 | 7.366E-03 | 5.525E-05 | 2.709E+08 | 1.509E+07 | 6.347E-02 | 2.525E+07 | 2.842E-01 |
| 117 | RH-03T | 3 | T3 | 8.890E-02 | 7.620E-03 | 6.182E-05 | 2.458E+08 | 1.545E+07 | 7.308E-02 | 2.355E+07 | 2.814E-01 |
| 118 | RH-03T | 5 | T5 | 8.890E-02 | 7.620E-03 | 7.188E-05 | 2.020E+08 | 1.353E+07 | 7.342E-02 | 2.111E+07 | 2.834E-01 |
| 119 | RH-03T | 6 | T6 | 8.890E-02 | 8.128E-03 | 7.864E-05 | 3.510E+08 | 1.257E+07 | 5.820E-02 | 3.746E+07 | 2.926E-01 |
| 120 | RH-03T | 7 | T7 | 8.890E-02 | 8.128E-03 | 8.656E-05 | 2.871E+08 | 1.287E+07 | 5.211E-02 | 2.084E+07 | 2.834E-01 |
| 121 | RH-03T | 10 | T10 | 8.890E-02 | 1.016E-02 | 1.244E-04 | 3.319E+08 | 1.255E+07 | 5.084E-02 | 1.895E+07 | 2.746E-01 |
| 122 | RH-03T | 11 | T11 | 8.890E-02 | 1.118E-02 | 1.449E-04 | 2.692E+08 | 1.043E+07 | 5.099E-02 | 1.787E+07 | 2.822E-01 |
| 123 | RH-03T | 12 | T12 | 8.890E-02 | 1.067E-02 | 1.646E-04 | 2.665E+08 | 1.108E+07 | 5.336E-02 | 1.662E+07 | 2.825E-01 |
| 124 | RH-03T | 13 | L1 | 8.890E-02 | 1.346E-02 | 1.772E-04 | 2.991E+08 | 1.062E+07 | 4.302E-02 | 1.793E+07 | 2.732E-01 |
| 125 | RH-03T | 14 | L2 | 8.890E-02 | 1.524E-02 | 2.033E-04 | 3.418E+08 | 8.988E+06 | 3.483E-02 | 1.749E+07 | 2.527E-01 |
| 126 | RH-03T | 15 | L3 | 8.890E-02 | 1.600E-02 | 2.033E-04 | 3.882E+08 | 1.083E+07 | 3.635E-02 | 1.991E+07 | 2.578E-01 |
| 127 | RH-03T | 17 | L5 | 8.890E-02 | 1.803E-02 | 2.368E-04 | 3.296E+08 | 9.479E+06 | 3.636E-02 | 1.634E+07 | 2.800E-01 |
| 128 | RH-03T | 18 | L6 | 8.890E-02 | 1.676E-02 | 2.362E-04 | 2.689E+08 | 9.425E+06 | 4.176E-02 | 1.529E+07 | 2.474E-01 |
| 129 | RH-03Y | 1 | T1 | 8.890E-02 | 5.334E-03 | 7.409E-05 | 1.548E+08 | 1.072E+07 | 9.131E-02 | 1.815E+07 | 2.842E-01 |
| 130 | RH-03Y | 2 | T2 | 8.890E-02 | 6.096E-03 | 6.846E-05 | 2.111E+08 | 1.462E+07 | 9.583E-02 | 2.047E+07 | 2.187E-01 |
| 131 | RH-03Y | 3 | T3 | 8.890E-02 | 6.096E-03 | 7.388E-05 | 1.560E+08 | 1.587E+07 | 1.217E-01 | 2.061E+07 | 2.176E-01 |
| 132 | RH-03Y | 5 | T5 | 8.890E-02 | 6.604E-03 | 8.311E-05 | 1.980E+08 | 1.416E+07 | 1.005E-01 | 1.857E+07 | 1.659E-01 |
| 133 | RH-03Y | 6 | T6 | 8.890E-02 | 6.604E-03 | 8.668E-05 | 1.960E+08 | 1.403E+07 | 9.693E-02 | 1.807E+07 | 1.623E-01 |
| 134 | RH-03Y | 7 | T7 | 8.890E-02 | 6.858E-03 | 9.024E-05 | 1.947E+08 | 1.494E+07 | 9.613E-02 | 1.802E+07 | 1.406E-01 |
| 135 | RH-03Y | 10 | T10 | 8.890E-02 | 8.382E-03 | 1.430E-04 | 2.288E+08 | 1.258E+07 | 6.678E-02 | 1.511E+07 | 1.183E-01 |
| 136 | RH-03Y | 11 | T11 | 8.890E-02 | 9.652E-03 | 1.534E-04 | 2.391E+08 | 1.299E+07 | 7.289E-02 | 1.658E+07 | 1.511E-01 |
| 137 | RH-03Y | 12 | T12 | 8.890E-02 | 1.067E-02 | 1.795E-04 | 1.968E+08 | 1.073E+07 | 7.077E-02 | 1.436E+07 | 1.434E-01 |
| 138 | RH-03Y | 13 | L1 | 8.890E-02 | 1.219E-02 | 1.994E-04 | 2.090E+08 | 1.130E+07 | 7.122E-02 | 1.506E+07 | 1.592E-01 |
| 139 | RH-03Y | 14 | L2 | 8.890E-02 | 1.346E-02 | 2.090E-04 | 2.947E+08 | 1.128E+07 | 5.179E-02 | 1.524E+07 | 1.310E-01 |
| 140 | RH-03Y | 15 | L3 | 8.890E-02 | 1.448E-02 | 2.335E-04 | 2.186E+08 | 9.586E+06 | 5.263E-02 | 1.449E+07 | 1.623E-01 |
| 141 | RH-03Y | 17 | L5 | 8.890E-02 | 1.575E-02 | 2.507E-04 | 2.279E+08 | 9.209E+06 | 4.871E-02 | 1.329E+07 | 1.959E-01 |
| 142 | RH-03Y | 18 | L6 | 8.890E-02 | 1.499E-02 | 2.637E-04 | 2.178E+08 | 8.214E+06 | 5.203E-02 | 1.399E+07 | 2.266E-01 |
| 143 | RH-Y8296 | 10 | T10 | 8.890E-02 | 1.041E-02 | .401E-04 | 1.856E+08 | 1.195E+07 | 1.249E-01 | 1.616E+07 | 2.925E-01 |
| 144 | RH-Y8296 | 11 | T11 | 8.890E-02 | 1.169E-02 | ..580E-04 | 3.000E+08 | 9.930E+06 | 3.962E-02 | 1.440E+07 | 2.842E-01 |
| 145 | RH-Y8296 | 12 | T12 | 8.890E-02 | 1.270E-02 | 1.727E-04 | 2.335E+08 | 1.021E+07 | 5.570E-02 | 1.646E+07 | 2.787E-01 |
| 146 | RH-Y8296 | 13 | L1 | 8.890E-02 | 1.448E-02 | 1.984E-04 | 3.296E+08 | 9.037E+06 | 3.623E-02 | 1.560E+07 | 2.801E-01 |
| 147 | RH-Y8296 | 14 | L2 | 8.890E-02 | 1.626E-02 | 2.213E-04 | 3.072E+08 | 8.622E+06 | 3.859E-02 | 1.588E+07 | 2.050E-01 |
| 148 | RH-Y8296 | 15 | L3 | 8.890E-02 | 1.702E-02 | 2.328E-04 | 2.967E+08 | 7.744E+06 | 3.181E-02 | 1.589E+07 | 2.225E-01 |
| 149 | RH-Y8296 | 17 | L5 | 8.890E-02 | 1.880E-02 | 2.473E-04 | 3.184E+08 | 6.893E+06 | 3.252E-02 | 1.758E+07 | 2.677E-01 |
| 150 | RH-Y8296 | 18 | L6 | 8.890E-02 | 1.803E-02 | 2.572E-04 | 3.301E+08 | 7.854E+06 | 3.327E-02 | 1.583E+07 | 2.643E-01 |

Table 1

| N | Subject ID | CP | OB Level | Displacement Rate m/s | Stiffness N/m | Yield Load N | Displacement to Yield Load m | Ultimate Load (Body) N | Displacement to Ultimate Load (Body) m | Energy to Ultimate Load (Body) Joule |
|---|---|---|---|---|---|---|---|---|---|---|
| 101 | RH-0F8 | 1 | T1 | 8.890E-02 | 1.910E+06 | 7.380E+02 | 5.013E-04 | 1.066E+03 | 1.511E-03 | 1.121E+00 |
| 102 | RH-0F8 | 2 | T2 | 8.890E-02 | 1.949E+06 | 8.218E+02 | 4.938E-04 | 1.100E+03 | 1.630E-03 | 1.375E+00 |
| 103 | RH-0F8 | 3 | T3 | 8.890E-02 | 2.217E+06 | 9.043E+02 | 5.202E-04 | 1.149E+03 | 1.733E-03 | 1.505E+00 |
| 104 | RH-0F8 | 5 | T5 | 8.890E-02 | 2.921E+06 | 1.026E+03 | 3.871E-04 | 1.176E+03 | 1.733E-03 | 1.735E+00 |
| 105 | RH-0F8 | 6 | T6 | 8.890E-02 | 2.414E+06 | 1.039E+03 | 5.131E-04 | 1.273E+03 | 8.206E-04 | 6.119E-01 |
| 106 | RH-0F8 | 7 | T7 | 8.890E-02 | 4.000E+06 | 1.134E+03 | 4.052E-04 | 1.429E+03 | 7.354E-04 | 6.225E-01 |
| 107 | RH-0F8 | 10 | T10 | 8.890E-02 | 3.652E+06 | 1.575E+03 | 5.963E-04 | 1.959E+03 | 1.922E-03 | 2.866E+00 |
| 108 | RH-0F8 | 11 | T11 | 8.890E-02 | 3.365E+06 | 1.471E+03 | 5.674E-04 | 1.949E+03 | 2.618E-03 | 4.087E+00 |
| 109 | RH-0F8 | 12 | T12 | 8.890E-02 | 3.037E+06 | 1.515E+03 | 6.353E-04 | 2.233E+03 | 2.134E-03 | 3.418E+00 |
| 110 | RH-0F8 | 13 | L1 | 8.890E-02 | 3.199E+06 | 1.773E+03 | 7.858E-04 | 2.724E+03 | 2.805E-03 | 5.403E+00 |
| 111 | RH-0F8 | 14 | L2 | 8.890E-02 | 5.189E+06 | 2.111E+03 | 5.890E-04 | 2.751E+03 | 2.126E-03 | 4.432E+00 |
| 112 | RH-0F8 | 15 | L3 | 8.890E-02 | 5.886E+06 | 2.305E+03 | 5.105E-04 | 3.056E+03 | 2.682E-03 | 6.688E+00 |
| 113 | RH-0F8 | 17 | L5 | 8.890E-02 | 5.941E+06 | 2.713E+03 | 6.274E-04 | 3.414E+03 | 2.971E-03 | 8.472E+00 |
| 114 | RH-0F8 | 18 | L6 | 8.890E-02 | 5.178E+06 | 2.445E+03 | 7.582E-04 | 3.118E+03 | 3.451E-03 | 8.788E+00 |
| 115 | RH-03T | 1 | T1 | 8.890E-02 | 1.399E+06 | 8.416E+02 | 7.852E-04 | 3.155E+03 | 1.731E-03 | 1.536E+00 |
| 116 | RH-03T | 2 | T2 | 8.890E-02 | 2.032E+06 | 8.336E+02 | 4.676E-04 | 1.395E+03 | 2.093E-03 | 2.061E+00 |
| 117 | RH-03T | 3 | T3 | 8.890E-02 | 1.994E+06 | 9.553E+02 | 5.569E-04 | 1.456E+03 | 2.144E-03 | 2.197E+00 |
| 118 | RH-03T | 5 | T5 | 8.890E-02 | 1.905E+06 | 9.726E+02 | 5.594E-04 | 1.513E+03 | 2.160E-03 | 2.406E+00 |
| 119 | RH-03T | 6 | T6 | 8.890E-02 | 3.396E+06 | 9.885E+02 | 4.731E-04 | 2.946E+03 | 2.378E-03 | 2.975E+00 |
| 120 | RH-03T | 7 | T7 | 8.890E-02 | 3.057E+06 | 1.114E+03 | 4.235E-04 | 1.804E+03 | 2.303E-03 | 3.141E+00 |
| 121 | RH-03T | 10 | T10 | 8.890E-02 | 4.065E+06 | 1.561E+03 | 5.166E-04 | 2.345E+03 | 2.780E-03 | 5.122E+00 |
| 122 | RH-03T | 11 | T11 | 8.890E-02 | 3.491E+06 | 1.511E+03 | 5.699E-04 | 2.590E+03 | 3.154E-03 | 6.099E+00 |
| 123 | RH-03T | 12 | T12 | 8.890E-02 | 4.111E+06 | 1.823E+03 | 5.693E-04 | 2.725E+03 | 3.014E-03 | 6.363E+00 |
| 124 | RH-03T | 13 | L1 | 8.890E-02 | 3.936E+06 | 1.891E+03 | 5.791E-04 | 3.177E+03 | 3.679E-03 | 8.926E+00 |
| 125 | RH-03T | 14 | L2 | 8.890E-02 | 4.559E+06 | 1.827E+03 | 5.309E-04 | 3.557E+03 | 3.852E-03 | 1.016E+01 |
| 126 | RH-03T | 15 | L3 | 8.890E-02 | 4.933E+06 | 2.201E+03 | 5.817E-04 | 4.047E+03 | 4.125E-03 | 1.238E+01 |
| 127 | RH-03T | 17 | L5 | 8.890E-02 | 4.328E+06 | 2.245E+03 | 6.556E-04 | 3.868E+03 | 5.050E-03 | 1.521E+01 |
| 128 | RH-03T | 18 | L6 | 8.890E-02 | 3.790E+06 | 2.226E+03 | 7.001E-04 | 3.611E+03 | 4.148E-03 | 1.144E+01 |
| 129 | RH-03Y | 1 | T1 | 8.890E-02 | 2.150E+06 | 7.939E+02 | 4.870E-04 | 1.344E+03 | 1.516E-03 | 1.359E+00 |
| 130 | RH-03Y | 2 | T2 | 8.890E-02 | 2.371E+06 | 1.001E+03 | 5.842E-04 | 1.441E+03 | 1.339E-03 | 1.210E+00 |
| 131 | RH-03Y | 3 | T3 | 8.890E-02 | 1.891E+06 | 1.173E+03 | 7.422E-04 | 1.523E+03 | 1.326E-03 | 1.200E+00 |
| 132 | RH-03Y | 5 | T5 | 8.890E-02 | 2.491E+06 | 1.177E+03 | 6.638E-04 | 1.544E+03 | 1.096E-03 | 9.219E-01 |
| 133 | RH-03Y | 6 | T6 | 8.890E-02 | 2.572E+06 | 1.216E+03 | 6.401E-04 | 1.566E+03 | 1.072E-03 | 9.377E-01 |
| 134 | RH-03Y | 7 | T7 | 8.890E-02 | 2.562E+06 | 1.348E+03 | 6.593E-04 | 1.626E+03 | 9.641E-04 | 8.466E-01 |
| 135 | RH-03Y | 10 | T10 | 8.890E-02 | 3.903E+06 | 1.799E+03 | 5.598E-04 | 2.160E+03 | 9.916E-04 | 1.347E+00 |
| 136 | RH-03Y | 11 | T11 | 8.890E-02 | 3.802E+06 | 1.993E+03 | 7.026E-04 | 2.544E+03 | 1.458E-03 | 2.386E+00 |
| 137 | RH-03Y | 12 | T12 | 8.890E-02 | 3.312E+06 | 1.927E+03 | 7.550E-04 | 2.577E+03 | 1.530E-03 | 2.464E+00 |
| 138 | RH-03Y | 13 | L1 | 8.890E-02 | 3.419E+06 | 2.253E+03 | 8.684E-04 | 3.004E+03 | 1.942E-03 | 3.758E+00 |
| 139 | RH-03Y | 14 | L2 | 8.890E-02 | 4.575E+06 | 2.356E+03 | 6.972E-04 | 3.185E+03 | 1.764E-03 | 3.786E+00 |
| 140 | RH-03Y | 15 | L3 | 8.890E-02 | 3.526E+06 | 2.239E+03 | 7.620E-04 | 3.384E+03 | 2.349E-03 | 5.559E+00 |
| 141 | RH-03Y | 17 | L5 | 8.890E-02 | 3.628E+06 | 2.309E+03 | 7.671E-04 | 3.332E+03 | 3.085E-03 | 7.664E+00 |
| 142 | RH-03Y | 18 | L6 | 8.890E-02 | 3.832E+06 | 2.166E+03 | 7.798E-04 | 3.689E+03 | 3.396E-03 | 9.046E+00 |
| 143 | RH-Y8296 | 10 | T10 | 8.890E-02 | 2.496E+06 | 1.674E+03 | 1.301E-03 | 2.263E+03 | 2.952E-03 | 4.011E+00 |
| 144 | RH-Y8296 | 11 | T11 | 8.890E-02 | 4.057E+06 | 1.569E+03 | 4.629E-04 | 2.275E+03 | 3.320E-03 | 6.211E+00 |
| 145 | RH-Y8296 | 12 | T12 | 8.890E-02 | 3.176E+06 | 1.764E+03 | 7.074E-04 | 2.842E+03 | 3.539E-03 | 7.392E+00 |
| 146 | RH-Y8296 | 13 | L1 | 8.890E-02 | 4.516E+06 | 1.793E+03 | 5.245E-04 | 3.094E+03 | 4.055E-03 | 9.500E+00 |
| 147 | RH-Y8296 | 14 | L2 | 8.890E-02 | 4.183E+06 | 1.908E+03 | 6.274E-04 | 3.515E+03 | 3.332E-03 | 8.172E+00 |
| 148 | RH-Y8296 | 15 | L3 | 8.890E-02 | 4.060E+06 | 1.803E+03 | 5.413E-04 | 3.699E+03 | 3.786E-03 | 1.013E+01 |
| 149 | RH-Y8296 | 17 | L5 | 8.890E-02 | 4.188E+06 | 1.704E+03 | 6.112E-04 | 4.346E+03 | 5.031E-03 | 1.532E+01 |
| 150 | RH-Y8296 | 18 | L6 | 8.890E-02 | 4.707E+06 | 2.020E+03 | 6.001E-04 | 4.072E+03 | 4.766E-03 | 1.388E+01 |

Table 2

VERTEBRAL CENTRUM COMPRESSION TEST, SPINAL LEVEL EFFECT ON STRENGTH PARAMETER, POSITION GROUPING ACCORDING TO INCREASING VALUE, DASHES (-) INDICATE SIGNIFICANT STATISTICAL DIFFERANCE BETWEEN EACH AND EVERY COLUMN POSITION SEPARATED BY A DASH ($\alpha = 0.05$)

| | RC | RK |
|---|---|---|
| Stiffness | $P_1P_2\text{-}P_4\text{-}P_5P_6$ | $P_1\text{-}P_2\text{-}P_4\text{-}P_5P_6$ |
| Yield Load | $P_1P_2\text{-}P_4\text{-}P_5P_6$ | $P_1P_2\text{-}P_4\text{-}P_5P_6$ |
| Disp. to Yield Load | $P_1P_2\text{-}P_4P_5P_6$ | $P_2P_1P_5P_4P_6$ |
| Ultimate Load | $P_1P_2\text{-}P_4\text{-}P_5P_6$ | $P_1\text{-}P_2\text{-}P_4\text{-}P_5\text{-}P_6$ |
| Disp. to Ult. Load | $P_2P_1P_4\ P_5\text{-}P_6$ | $P_2P_1\text{-}P_4\text{-}P_5\text{-}P_6$ |
| Energy to Ult. Load | $P_1P_2P_4\text{-}P_5\text{-}P_6$ | $P_2P_1\text{-}P_4\text{-}P_5\text{-}P_6$ |
| Modulus | $P_1P_4P_2\text{-}P_6P_5$ | $P_4P_1P_2P_6P_5$ |
| Yield Stress | $P_6\text{-}P_4P_5\ P_2P_1$ | $P_6P_5\text{-}P_4\text{-}P_2\text{-}P_1$ |
| Ultimate Stress | $P_6\text{-}P_4P_5P_2\text{-}P_1$ | $P_6P_5P_4P_2P_1$ |
| Yield Strain | $P_6P_5\text{-}P_4\text{-}P_2P_1$ | $P_6P_5\text{-}P_4\text{-}P_2P_1$ |
| Ultimate Strain | $P_5P_6P_4\text{-}P_2P_1$ | $P_2P_5P_4P_6P_1$ |

Table 3

Figure 1

Illustrating potting procedure with vertebral body sitting on the methylmethacrylate thin pot

PHYSICAL INTERVERTEBRAL DISC MEASUREMENTS FOR KETAMINE EXPOSURE GROUP, MEAN (X) AND STANDARD DEVIATION (S)

| DISC LEVEL | ANTERIOR HEIGHT (mm) | | POSTERIOR HEIGHT (mm) | | WATER WEIGHT LOSS PERCENT | | WATER WT/VOLUME PERCENT/$cm^3$ | |
|---|---|---|---|---|---|---|---|---|
| | X | S | X | S | X | S | X | S |
| T4-5 | 3.10 | .33 | 2.04 | .54 | 54.43 | 2.37 | 158.61 | 28.14 |
| T7-8 | 3.54 | .51 | 2.21 | .39 | 54.45 | 2.81 | 103.31 | 22.27 |
| T9-10 | 4.68 | .85 | 2.46 | .63 | 55.03 | 2.67 | 64.41 | 8.70 |
| T11-12 | 5.5 | .62 | 2.84 | .19 | 56.93 | 3.34 | 41.39 | 4.96 |
| L1-2 | 5.73 | .83 | 3.29 | .85 | 58.18 | 2.94 | 30.85 | 5.13 |
| L4-5 | 6.51 | .40 | 3.20 | .79 | 57.78 | 2.67 | 22.10 | 2.62 |
| L6-7 | 7.00 | .97 | 3.61 | 1.28 | 57.55 | 3.02 | 20.58 | 6.22 |

Table 4

# INTERVERTEBRAL DISC HYDRATION ANALYSIS

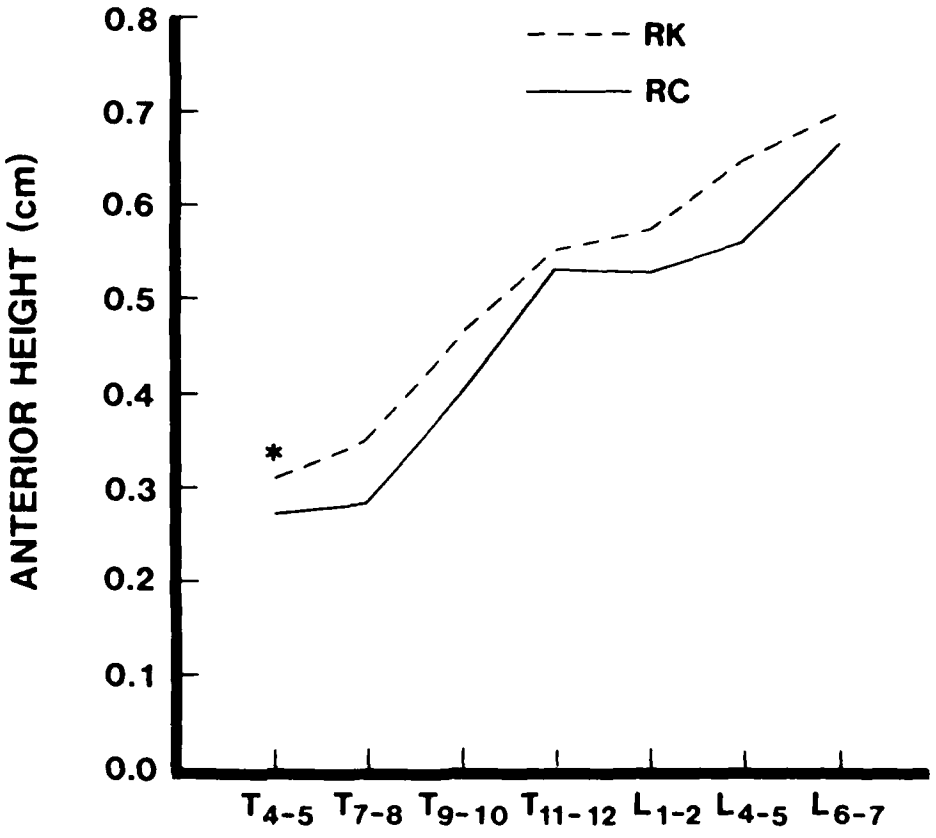


Figure 2

# INTERVERTEBRAL DISC HYDRATION ANALYSIS

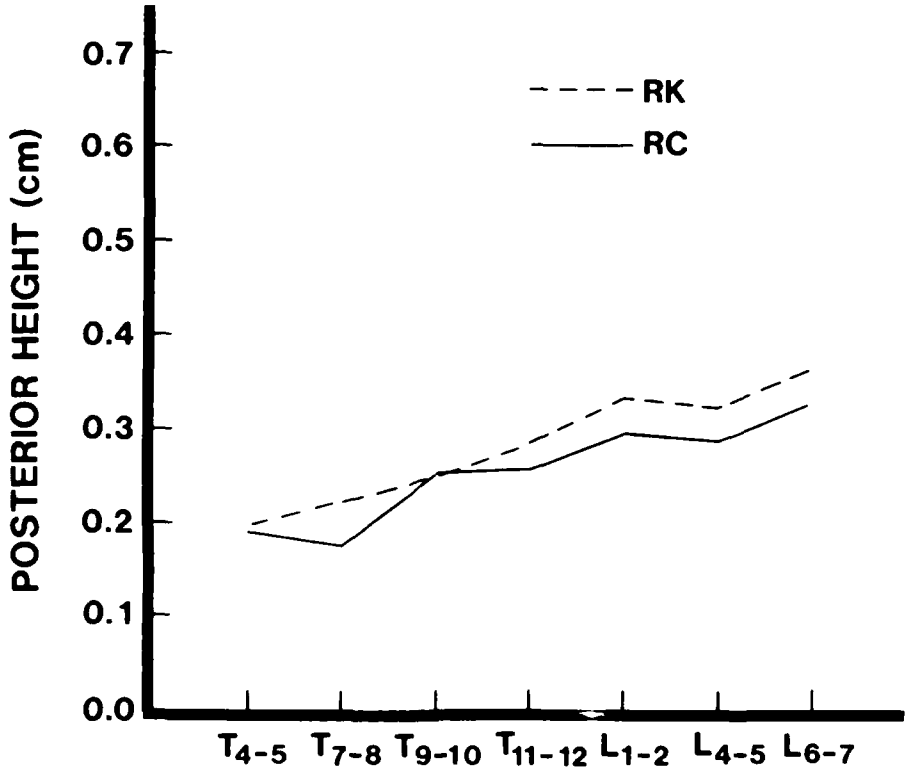


Figure 3

# INTERVERTEBRAL DISC HYDRATION ANALYSIS

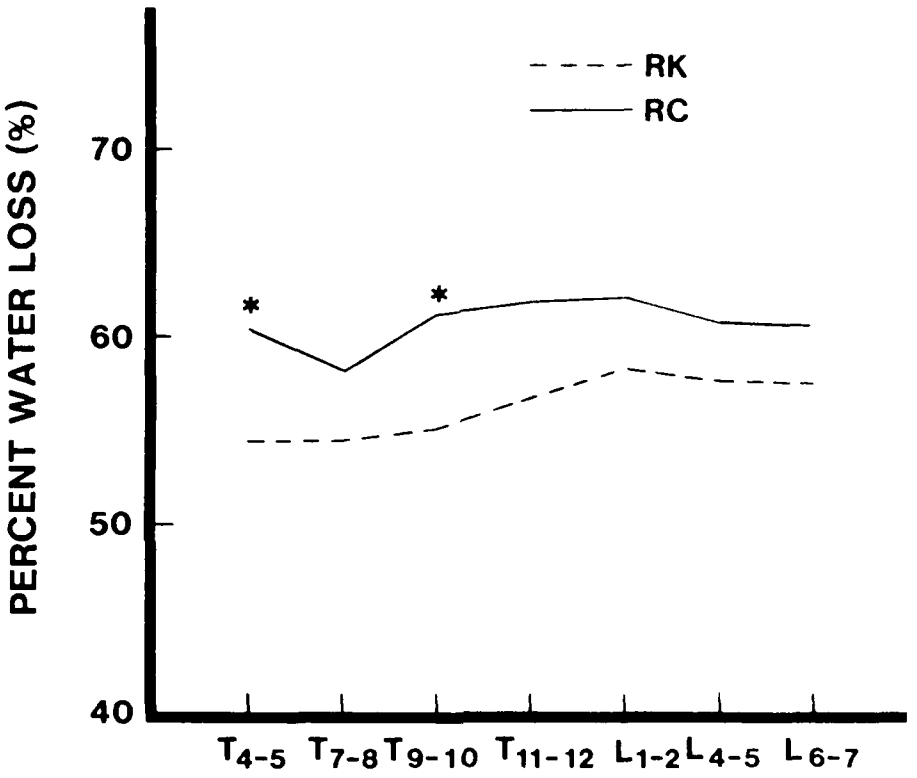


Figure 4

# INTERVERTEBRAL DISC HYDRATION ANALYSIS

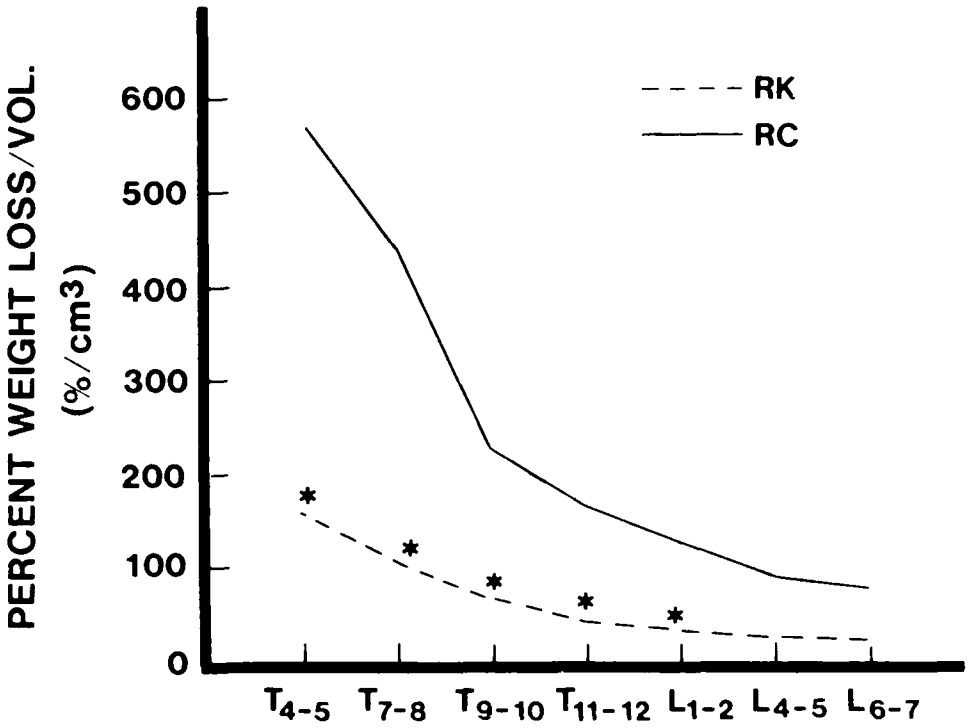


Figure 5

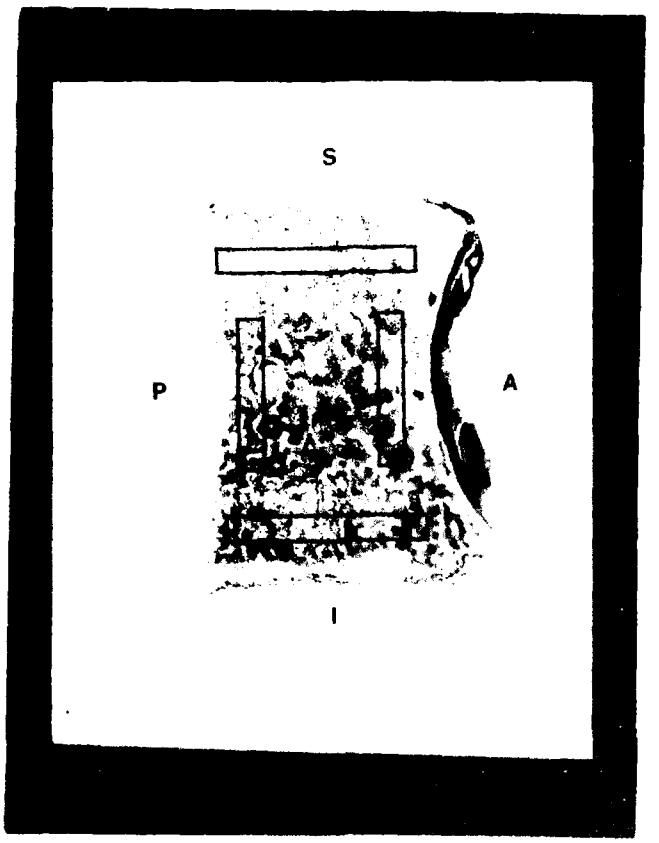


Figure 6

Lumbar 4 Tissue Section Illustrating Analysis Sites,
Superior (S), Anterior (A), Posterior (P) and Inferior (I)

BONE HISTOMORPHOMETRY, LUMBAR 4 MIDSAGITTAL VERTEBRAL CENTRUM ANALYSIS, MEAN (X), STANDARD DEVIATION (S) AND SAMPLE NUMBER (N) FOR THE ANTERIOR REGION

| PARAMETERS | RC | | | RK | | |
|---|---|---|---|---|---|---|
| | x | s | n | x | s | n |
| VV | 402.21 | 230.48 | 20 | 169.30 | 50.25 | 48* |
| SV | 2843.38 | 1318.18 | 20 | 3425.05 | 892.56 | 48* |
| DTRAB | 723.68 | 566.61 | 20 | 262.89 | 104.46 | 48* |
| VVOS | 6.16 | 7.57 | 20 | 18.78 | 20.29 | 48* |
| THOS | 13.10 | 6.26 | 21 | 20.30 | 18.83 | 48* |
| OSI | 21.20 | 28.02 | 20 | 17.22 | 15.77 | 48 |
| VVOI | 15.93 | 22.79 | 20 | 113.73 | 128.21 | 48* |
| HL | 6.91 | 10.41 | 20 | 11.16 | 15.61 | 48 |

*Indicates significant difference (ANOVA, $\alpha$=0.05)

Table 5

BONE HISTOMORPHOMETRY, LUMBAR 4 MIDSAGITTAL VERTEBRAL CENTRUM ANALYSIS, MEAN (X), STANDARD DEVIATION (S) AND SAMPLE NUMBER (N) FOR THE INFERIOR REGION

| PARAMETERS | RC | | | RK | | |
|---|---|---|---|---|---|---|
| | x | s | n | x | s | n |
| VV | 260.41 | 102.34 | 24 | 183.09 | 45.85 | 100* |
| SV | 6394.44 | 1480.30 | 24 | 3910.10 | 752.05 | 100* |
| DTRAB | 216.06 | 97.90 | 24 | 250.17 | 103.54 | 100 |
| VVOS | 9.97 | 8.73 | 24 | 3.87 | 2.28 | 100* |
| THOS | 8.70 | 4.29 | 85 | 100.73 | 170.57 | 100* |
| OSI | 18.39 | 11.30 | 24 | 7.68 | 4.49 | 100* |
| VVOI | 35.43 | 29.70 | 24 | 20.12 | 7.28 | 100* |
| HL | 8.01 | 6.80 | 24 | 12.97 | 5.04 | 100* |

*Indicates significant difference (ANOVA, $\alpha$=0.05)

Table 6

BONE HISTOMORPHOMETRY, LUMBAR 4 MIDSAGITTAL VERTEBRAL CENTRUM ANALYSIS, MEAN (X), STANDARD DEVIATION (S) AND SAMPLE NUMBER (N) FOR THE SUPERIOR REGION

| PARAMETERS | RC | | | RK | | |
|---|---|---|---|---|---|---|
| | x | s | n | x | s | n |
| VV | 245.71 | 66.56 | 24 | 155.36 | 51.58 | 100* |
| SV | 6230.99 | 1058.68 | 24 | 4249.07 | 1698.14 | 100* |
| DTRAB | 202.64 | 65.74 | 24 | 196.18 | 43.03 | 100 |
| VVOS | 10.30 | 5.38 | 24 | 9.39 | 8.88 | 100 |
| THOS | 8.99 | 4.40 | 95 | 15.02 | 1.22 | 100* |
| OSI | 21.74 | 9.37 | 24 | 15.44 | 11.65 | 100* |
| VVOI | 41.84 | 25.45 | 24 | 52.27 | 36.37 | 100 |
| HL | 8.72 | 6.04 | 24 | 7.39 | 5.04 | 100 |

*Indicates significant difference (ANOVA, $\alpha = 0.05$)

Table 7

BONE HISTOMORPHOMETRY, LUMBAR 4 MIDSAGITTAL VERTEBRAL CENTRUM ANALYSIS, MEAN (X), STANDARD DEVIATION (S) AND SAMPLE NUMBER (N) FOR THE POSTERIOR REGION

| PARAMETERS | RC | | | RK | | |
|---|---|---|---|---|---|---|
| | x | s | n | x | s | n |
| VV | 247.07 | 131.3 | 20 | 134.48 | 43.42 | 48* |
| SV | 5179.57 | 2236.82 | 20 | 4418.31 | 1597.64 | 48 |
| DTRAB | 254.14 | 169.91 | 20 | 158.56 | 29.23 | 48* |
| VVOS | 5.86 | 5.92 | 20 | 4.86 | 2.95 | 48 |
| THOS | 6.99 | 3.79 | 65 | 16.18 | 1.55 | 48* |
| OSI | 17.44 | 12.49 | 20 | 11.82 | 11.37 | 48* |
| VVOI | 21.76 | 20.49 | 20 | 48.42 | 51.15 | 48* |
| HL | 9.04 | 7.53 | 20 | 8.97 | 8.72 | 48* |

*Indicates significant difference (ANOVA, $\alpha$=0.05)

Table 8

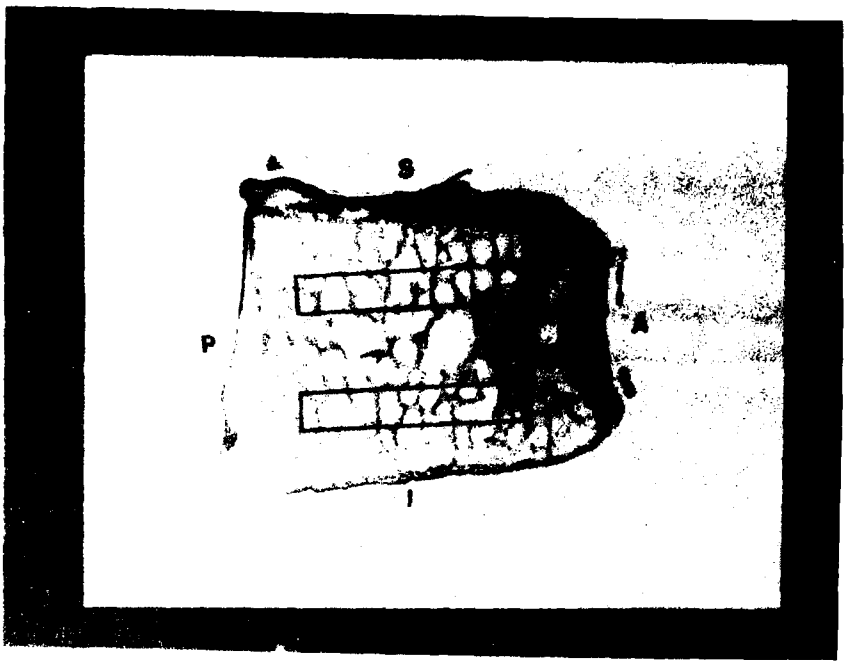


Figure 7

Thoracic 9 Tissue Section Illustrating Analysis Sites Superior (S) and Inferior (I)

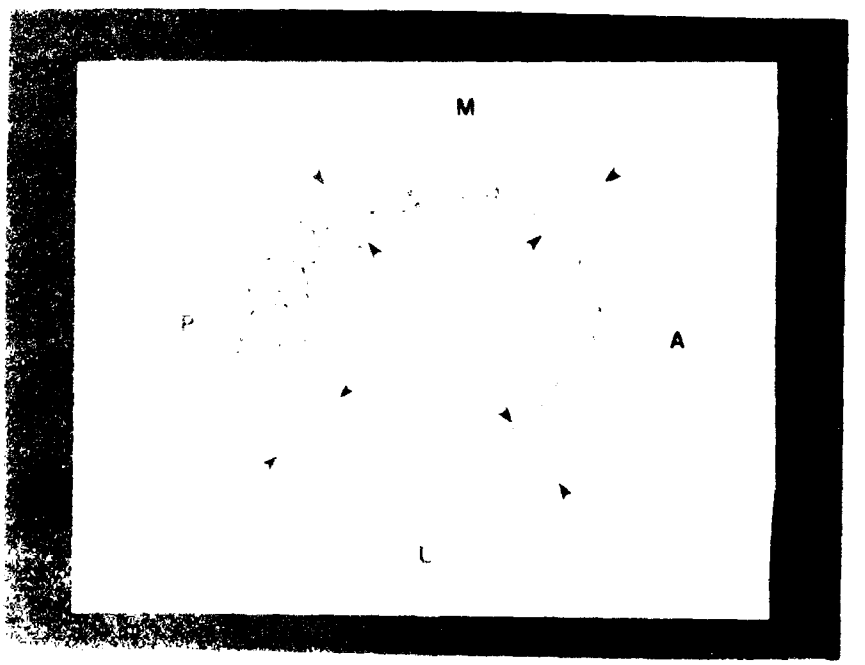


Figure 8

Cortical Bone Tissue Sections Illustrating Quadrant Analysis Sites Medial (M), Posterior (P), Anterior (A) and Lateral (L)

BONE HISTOMORPHOMETRY, THORACIC 9 MIDSAGITTAL VERTEBRAL CENTRUM ANALYSIS, MEAN (X), STANDARD DEVIATION (S) AND SAMPLE NUMBER (N) FOR THE SUPERIOR REGION

| PARAMETERS | RC | | | RK | | |
|---|---|---|---|---|---|---|
| | x | s | n | x | s | n |
| VV | 253.98 | 86.25 | 18 | 202.63 | 66.80 | 72* |
| SV | 5135.19 | 1029.02 | 18 | 4420.35 | 710.62 | 72* |
| DTRAB | 250.62 | 89.61 | 18 | 231.49 | 56.40 | 72 |
| VVOS | 3.25 | 2.01 | 18 | 3.99 | 1.79 | 72* |
| THOS | 6.63 | 3.09 | 37 | 23.41 | 6.32 | 72* |
| OSI | 11.59 | 7.05 | 18 | 5.30 | 2.47 | 72* |
| VVOI | 12.88 | 9.05 | 18 | 22.96 | 15.49 | 72* |
| HL | 6.70 | 5.59 | 18 | 16.12 | 7.61 | 72* |

*Indicates significant difference (ANOVA, [illegible])

BONE HISTOMORPHOMETRY, THORACIC 9 MIDSAGITTAL VERTEBRAL CENTRUM ANALYSIS, MEAN (X), STANDARD DEVIATION (S) AND SAMPLE NUMBER (N) FOR THE INFERIOR REGION

| PARAMETERS | RC | | | RK | | |
|---|---|---|---|---|---|---|
| | x | s | n | x | s | n |
| VV | 269.98 | 109.14 | 18 | 177.32 | 33.75 | 72* |
| SV | 6332.64 | 1848.61 | 18 | 4737.18 | 801.82 | 72* |
| DTRAB | 215.82 | 98.71 | 18 | 190.62 | 17.59 | 72* |
| VVOS | 4.35 | 3.43 | 18 | 5.15 | 3.04 | 72 |
| THOS | 7.49 | 3.83 | 47 | 18.35 | 1.76 | 72* |
| OSI | 11.29 | 8.69 | 18 | 7.41 | 3.08 | 72* |
| VVOI | 16.80 | 14.10 | 18 | 28.36 | 13.97 | 72* |
| HL | 5.11 | 2.43 | 18 | 7.59 | 3.17 | 72* |

*Indicates significant difference (ANOVA, $\alpha$=0.05)

Table 10

BONE HISTOMORPHOMETRY FEMORAL MIDSHAFT CORTICAL BONE ANALYSIS
MEANS (X) AND STANDARD DEVIATION (S) FOR THE LATERAL QUADRANT

| PARAMETER | EXPERIMENTAL GROUP | | | |
|---|---|---|---|---|
| | RC (N=3) | | RK (N=4) | |
| | X | S | X | S |
| BONE CROSS SECTIONAL AREA, mm ($A_c$) | 9.92 | 0.33 | 12.510 | 2.270 |
| NO. OSTEOID SEAMS/mm ($A_f$) | .798 | 1.12 | .676 | 1.210 |
| NO. RESORPTION SPACES/mm ($A_r$) | 1.00 | .173 | 0 | 0* |
| MEAN WALL THICKNESS, mm (mwt) | .044 | .021 | .018 | .002* |
| CIRCUM. OF OSTEOID SEAM, mm ($S_f$) | .239 | .247 | .055 | .071 |

*Indicates significant difference (ANOVA, $\alpha$=0.05)

Table 11

BONE HISTOMORPHOMETRY, FEMORAL MIDSHAFT CORTICAL BONE ANALYSIS
MEANS (X) AND STANDARD DEVIATIONS (S) FOR THE MEDIAL QUADRANT

| PARAMETER | EXPERIMENTAL GROUP | | | |
|---|---|---|---|---|
| | RC (N=3) | | RK (N=4) | |
| | X | S | X | S |
| BONE CROSS SECTIONAL AREA, mm ($A_c$) | 10.4 | 1.55 | 13.613 | 1.609* |
| NO. OSTEOID SEAMS/mm ($A_f$) | .120 | .049 | 3.2476 | 2.563* |
| NO. RESORPTION SPACES/mm ($A_r$) | .233 | .261 | 1.053 | .931 |
| MEAN WALL THICKNESS, mm (mwt) | .055 | .043 | .041 | .017 |
| CIRCUM. OF OSTEOID SEAM, mm ($S_f$) | .093 | .062 | .010 | .005* |

*Indicates significant difference (ANOVA, $\alpha$=0.05)

Table 12

BONE HISTOMORPHOMETRY FEMORAL MIDSHAFT CORTICAL BONE ANALYSIS
MEANS (X) AND STANDARD DEVIATION (S) FOR THE POSTERIOR QUADRANT

| PARAMETER | EXPERIMENTAL GROUP | | | |
|---|---|---|---|---|
| | RC (N=3) | | RK (N=4) | |
| | X | S | X | S |
| BONE CROSS SECTIONAL AREA, $mm^2$ ($A_c$) | 11.2 | 0.63 | 14.364 | 1.921* |
| NO. OSTEOID SEAMS/$mm^2$ ($A_f$) | 2.12 | 1.24 | 5.663 | 3.053 |
| NO. RESORPTION SPACES/$mm^2$ ($A_r$) | 0.75 | 0.49 | 1.501 | 1.050 |
| MEAN WALL THICKNESS, mm (mwt) | 0.068 | .012 | .046 | .019 |
| CIRCUM. OF OSTEOID SEAM, mm ($S_f$) | .013 | .010 | .004 | .001 |

*Indicates significant difference (ANOVA, $\alpha$=0.05)

Table 13

BONE HISTOMORPHOMETRY, FEMORAL MIDSHAFT CORTICAL BONE ANALYSIS
MEANS (X) AND STANDARD DEVIATIONS (S) FOR THE ANTERIOR QUADRANT

| PARAMETER | EXPERIMENTAL GROUP | | | |
|---|---|---|---|---|
| | RC (N=3) | | RK (N=4) | |
| | X | S | X | S |
| BONE CROSS SECTIONAL AREA, $mm^2$ ($A_c$) | 9.8 | 0.67 | 13.097 | 1.163* |
| NO. OSTEOID SEAMS/$mm^2$ ($A_f$) | .292 | .424 | 0.781 | .565 |
| NO. RESORPTION SPACES/$mm^2$ ($A_r$) | .033 | .058 | .537 | .351* |
| MEAN WALL THICKNESS, mm (mwt) | .045 | .020 | .032 | .014 |
| CIRCUM. OF OSTEOID SEAM, mm ($S_f$) | .230 | .293 | .046 | .035 |

*Indicates significant difference (ANOVA, $\alpha$=0.05)

Table 14

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